IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Schnellmann *et al.*	§	ART UNIT:
	§	1614
FILED: July 5, 2001	§	
	§	EXAMINER:
SERIAL NO.: 09/899,704	§	Cook, R
	§	
FOR: Use of Ascorbic Acid and Salts of Ascorbic Acid to Promote Cell Repair and Regeneration after Injury	§	DOCKET:
	§	D6305

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

ATTENTION: Board of Patent Appeals and Interferences

TRANSMITTAL OF APPEAL BRIEF

Dear Sir:

Enclosed please find three (3) originals of the Appeal Brief for the above-referenced patent application. Additionally, Applicants enclose a Petition for a Four Month Extension of Time under 37 C.F.R. 1.136.

This application was submitted on behalf of a small entity. A statement claiming Small Entity Status was included with the patent application. Please debit the $165 fee for filing a brief & $740 extension fee under 35 U.S.C. 1.17(a) & (c)) or any additional fees due from Deposit Account No. 07-1185 on which account the undersigned is allowed to draw.

Respectfully submitted,

Date: Nov 7, 2003

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APPELLANT'S BRIEF

This Brief is in furtherance of the Notice of Appeal filed in this case on May 8, 2003. The fees required under 37 C.F.R. §1.17(f) and any other required fees are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

In accordance with 37 C.F.R. §1.192(a), this Brief is submitted in triplicate.

INDEX OF SUBJECT MATTER

I. REAL PARTY IN INTEREST

The real party in interest is University of Arkansas For Medical Sciences, the Assignee, as evidenced by an Assignment recorded in the Patent and Trademark Office at Reel 012731, Frame 0825 on March 19, 2002.

II. RELATED APPEALS AND INTERFERENCES

Appellant is aware of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Originally claims 1-17 were filed with this Application. Claims 2, 5-10, 14 and 17 were canceled by amendment. The pending claims 1, 3-4, 11-13, 15-16 are being appealed of which claims 1, 11 and 15 are independent claims.

IV. STATUS OF AMENDMENTS

Subsequent to the Final Office Action mailed November 5, 2002, Applicant submitted a Response After Final which canceled claims 5-10 and 17 and amended claims 1, 11, 15-16. In the Advisory Action mailed April 23, 2003, the Examiner indicated that the proposed amendments will be entered upon appeal. All pending claims are shown in Appendix A.

V. SUMMARY OF THE INVENTION

The present invention was designed to test whether pharmacological concentrations of L-ascorbic acid phosphate can promote cellular recovery after injury induced by halocarbon nephrotoxicant such as dichlorovinyl-L-cysteine (page 35, lines 16-20; page 7, lines 2-5). It was demonstrated that ascorbic acid is a strong promoter of cell repair and regeneration, promoting cellular proliferation (page 27, line 14 to page 28, line 3), mitochondrial function (page 28, line 20 to page 29, line 4; page 29, line 17 to

page 30, line 1), Na^+-K^+-ATPase protein expression (page 32, line 13 to page 33, line 4), Na^+-K^+-ATPase protein activity and active Na^+ transport (page 30, lines 7-10; page 31, lines 3-5). The mechanism by which ascorbic acid produces this effect is not through its known antioxidant properties (see Abstract; page 7, line 7 to page 8, line 1). These results indicate that the beneficial effects of pharmacological concentrations of ascorbic acid are not limited to antioxidant action of this molecule and that ascorbic acid may be an important tool in promoting cellular recovery following toxicant-induced injury (page 8, lines 1-5).

VI. ISSUES

35 U.S.C. §103

Whether claims 1, 3-4, 11-13 and 15-16 are unpatentable over U.S. Pat. No. 4,711,780 (**Fahim**), U.S. Pat. No. 5,230,996 (**Rath**), **Saika** (abstract, 1993) or **Nowak** (abstract, 1997) alone or in combination under 35 U.S.C. §103(a).

VII. GROUPING OF CLAIMS

The rejected claims do stand or fall together.

VIII. ARGUMENTS

Rejection Under 35 U.S.C. §103

Claims 1, 3-4, 11-13, and 15-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. No. 4,711,780 (**Fahim**), U.S. Pat. No. 5,230,996 (**Rath**), **Saika** (abstract, 1993) or **Nowak** (abstract, 1997) alone or in combination. Applicants respectfully request that this rejection be reversed.

The present invention demonstrates that pharmacological concentrations of L-ascorbic acid phosphate (vitamin C) can promote cellular recovery after injury induced by a model halocarbon toxicant dichlorovinyl-L-cysteine. L-ascorbic acid phosphate promotes recovery of cellular proliferation, mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport. It is important to

note that the present invention teaches L-ascorbic acid phosphate acting alone is capable of promoting cellular recovery after injury caused by halocarbon toxicant.

In contrast, **Fahim** teaches a medication for the treatment of epithelial tissue comprising vitamin C, a zinc salt and a sulfur amino acid. **Rath** teaches a solution of ascorbate and tranexamic acid for the treatment or prevention of cardiovascular disease. **Fahim** and **Rath** only teach combinations of vitamin C and other compounds. **Fahim** and **Rath** do not teach or suggest vitamin C would be effective or useful when used alone as claimed herein. Hence, **Fahim** and **Rath** actually teach away from the instant invention.

Saika teaches the effect of ascorbic acid or ascorbic acid phosphate on alkali burns in the corneas of rabbits. The effects observed include an increase in non-burned stroma and basal lamina under new epithelia.

Nowak teaches ascorbic acid stimulates cellular regeneration in cells exposed to a model oxidant tert-butylhydroperoxide (TBHP). Ascorbic acid promoted regeneration

by stimulating proliferation and cell migration/spreading and decreasing cell death during the recovery period.

The Examiner contends that each of the cited prior art discloses that ascorbic acid phosphate and ascorbic acid promote recovery of cellular functions following injury caused by a variety of conditions, including toxic substances (Office Action mailed March 20, 2002, page 4). The Examiner concludes that the claims of the present invention differ from the cited prior art in reciting a specific toxic substance. According to the Examiner, once a method of using a compound is known to treat injury, no unobviousness is seen in an injury caused by a specific toxic substance (Office Action mailed March 20, 2002, page 4). Applicant respectfully disagrees.

Applicants respectfully submit that the Examiner has not provided clear evidentiary proof that demonstrates the required suggestion or motivation to modify the cited references to arrive at the instant invention. In contrast, the Examiner has only provided broad conclusory remarks without giving a reasoned argument based on the Graham factual inquiries.

To establish a *prima facie* case of obviousness, three

basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (M.P.E.P. §2143). Applicant submits that the Examiner has not met these three basic criteria.

First of all, there is no suggestion or motivation to modify any of the cited references to use L-ascorbic acid phosphate alone to recover mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport as claimed herein.

As discussed above, **Fahim** and **Rath** do not teach or suggest ascorbic acid phosphate would be effective or useful when used alone as claimed herein. Neither did **Fahim** and **Rath** teach or suggest recovery of mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport. **Saika** only teaches an effect based on the presence of basal lamina under new epithelia, whereas **Nowak** only teaches stimulation of

cell migration/spreading and decreasing cell death by ascorbic acid. Consequently, **Fahim**, **Rath**, **Saika** and **Nowak** do not teach or suggest all the claim limitations, and the combined references do not disclose anything related to recovery of mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport as claimed herein.

One of ordinary skill in the art would readily recognize that the cellular functions disclosed in **Fahim**, **Rath**, **Saika** and **Nowak** are different and distinct from those claimed in the present invention, and these different cellular functions may very well involve different cellular pathways. It is also well known in the art that a particular compound or agent may impact one cellular pathway but not the other. Therefore, absent any teaching or suggestion that the cellular functions/pathways disclosed in **Fahim**, **Rath**, **Saika** and **Nowak** and those claimed in the present invention share common features, one of ordinary skill in the art would not have the motivation and the requisite reasonable expectation of success to use ascorbic acid to recover mitochondrial function, Na^+-K^+-ATPase protein expression, Na^+-K^+-ATPase protein activity, and active Na^+ transport as claimed herein.

In view of the above remarks, Applicant submits that the combined teaching of **Fahim**, **Rath**, **Saika** and **Nowak** does not provide a person having ordinary skill in this art with the requisite expectation of successfully producing Applicant's claimed methods. The invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicant respectfully requests that the rejection of claims 1, 3-4, 11-13, and 15-16 under 35 U.S.C. §103(a) be withdrawn.

Respectfully submitted,

Date: Nov 6, 2003

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